TRANSLATION 03 IV 20 B

FAN/J7162 EP

German OLS 199 19 770 A1
Application filed: 30.4.1999
OLS published: 2.11.2000
Henkel KGaA

Use of nanoscale antimicrobial agents in oral and/or dental care

Nanoscale antimicrobial agents having a particle diameter in the range from 5 to 500 nm are used to prepare oral and dental care products, in particular toothpastes and dental gels. Compared with other forms known from the art, this fine particle size makes active agents easier to incorporate into formulations and makes them more effective.

Description

The invention relates to the use of antimicrobial agents in nanoscale form to prepare oral and/or dental care products.

Bacterial plaque is considered to be the main cause of caries and periodontal disease. This is why antimicrobial agents such as cetylpyridinium chloride, chlorhexidine, hexetidine, domiphen chloride, triclosan and sodium benzoate are used in oral and dental care. Clinical investigation has shown that formulations containing these agents can inhibit plaque formation and growth to some extent. From EP 0262587 there are known salicylamides which exhibit good activity against Gram-positive bacteria and which, because of their potency and their advantageous spectrum, are proposed as anti-plaque agents in oral and dental care compositions, for example mouthwashes and toothpastes. However, because they are sparingly-soluble, these salicylamides are so difficult to incorporate into the formulations that are used that the antibacterial effects they produce are not sufficient for practical purposes

Nanoscale substances are understood to be substances whose particle diameter in the largest direction is less than 1000 nm (nanometers). In this specification, the term "nanoparticulate" is used synonymously with "nanoscale".

Nanoscale active agents are described in the literature particularly as a means of obtaining the controlled release of an active agent over a prolonged period of time. For example, there are known from WO 98/114174 nanoparticles for therapeutic parenteral use which consist of a pharmacologically-active substance encapsulated in a shell of biodegradable polymer. As examples of pharmacologically active substances, there are mentioned inter alia antibacterial substances such as chloramphenicol and vancomycin as well as antimicrobial substances such as penicillins and cephalosporins.

Antimicrobial products containing nanoscale Schiff bases of aromatic aldehydes are known from DE 44 02 103 which describes the use of these products to obtain a long-lasting antimicrobial finish on textiles. Application CA 2,111,523 describes disinfectants which in addition to other components also contain surface-modified nanoparticulate antimicrobial agents. A disinfecting cleaner formulation is given as an example. Application CA 2,111,523 describes compositions with a long-lasting microbicidal action, which contain surface-modified nanoparticulate antimicrobial agents. As applications for these compositions, there are described surface disinfectants that provide lasting antimicrobially-active films on treated surfaces. However, there is nothing in the art to suggest that nanoparticulate antimicrobial substances can be advantageously used in oral and dental care. Although the skilled worker knows that antimicrobial agents are used for example for hard surface disinfection and in oral and dental care, he also knows that the type of use and the potency, spectrum of activity and the formulation of active agents in these different fields are so different that knowledge gained in one field cannot be simply transferred to another.

In practice, the problem with antimicrobial agents and in particular with sparingly water-soluble agents is that they are frequently difficult to incorporate into oral and/or dental care formulations and the resulting formulations have an unsatisfactory antimicrobial action. In addition, consumers need oral and/or dental care compositions that can contain smaller concentrations of active agent without sacrificing antibacterial action and which thus have health, economic and/or ecological advantages.

One aim of the invention is therefore to prepare oral and/or dental care compositions using antimicrobial agents whose poor solubility means they cannot be conventionally incorporated in an adequate concentration in oral and/or dental care compositions.

Another aim of the invention is to provide oral and/or dental care compositions which have sufficient antimicrobial action for practical use and which at the same time contain a smaller amount of antimicrobial agents.

This aim was achieved by using antimicrobial agents in the form of nanoparticles having a particle diameter in the range from 5 to 500 nm, preferably from 10 to 150 nm, to prepare oral and/or dental care compositions.

One object of the invention is therefore the use of nanoscale antimicrobial agents having a particle diameter in the range from 5 to 500 nm, and preferably from 10 to 150 nm, to prepare oral and/or dental care compositions in particular toothpastes or dental gels.

Surprisingly, it has been found that antimicrobial agents in nanoparticulate form are not only easier to incorporate into formulations for oral and/or dental care compositions, but that that their effectiveness also increases. This means that weight for weight, the nanoparticulate agent has a better antimicrobial action than the same agent in a larger particle size.

The use of antimicrobial agents in nanoparticulate form is especially useful if the agents are sparingly water-soluble or if they are not basic compounds and so cannot be converted into readily water-soluble salts by reaction with acids. Consequently, further embodiments of the invention relate to antimicrobial agents that are sparingly soluble in water and also to those which are not basic compounds.

The antimicrobial agents of the invention are preferably

- 4-Hydroxybenzoic acid, its alkali metal or alkaline earth metal salts or its esters with linear or branched alcohols with from 1 to 10 C atoms
- N-(4-chlorophenyl)-N'-(3,4-dichlorophenyl) urea

- 2,4,4'-Trichloro-2'-hydroxydiphenyl ether
- 4-Chloro-3,5-dimethylphenol
- 2,2'-Methylene-bis-(6-bromo-4-chlorophenol)
- 3-Methyl-4-(1-methylethyl)-phenol
- 2-Benzyl-4-chlorophenol
- 3-(4-chlorophenoxy)-1,2-propanediol
- 3-Iodo-2-propinylbutylcarbamate
- Vitamin A palmitate
- Thymol
- Salicylic acid-N-alkyl amides, wherein the alkyl groups have from 1 to 22 carbon atoms and can be linear or branched and mixtures thereof.

Especially preferred as antimicrobial active agents in accordance with the invention are salicylic acid N-octyl amide and/or salicylic acid N-decyl amide.

The nanoscale agents of the invention consist of a discrete phase of the agent on whose surface there is adsorbed preferably at least one surface-modifying substance. Emulsifiers and/or protective colloids are especially useful as surface-modifying substances. The result of coating the particles with emulsifiers and/or protective colloids is the absence of subsequent agglomeration.

As emulsifiers there are used for example nonionic surfactants chosen from at least one of the following groups:

(1) Addition products of from 2 to 30 moles of ethylene oxide and/or from 0 to 5 moles of propylene oxide with linear fatty alcohols having from 8 to 22 carbon atoms, fatty acids having from 12 to 22 carbon atoms, and alkylphenols with from 8 to 15 carbon atoms in the alkyl group;

(2) $C_{12/18}$ fatty acid mono and diesters of the addition products of from 1 to 30 moles of ethylene oxide and glycerol;

(3) Glycerol mono and diesters and sorbitan mono and diesters of saturated and unsaturated fatty acids having from 6 to 22 carbon atoms and their ethylene oxide addition products;

(4) Alkyl mono and oligoglycosides with from 8 to 22 carbon atoms in the alkyl group and their ethoxylated analogues;

(5) Addition products of from 15 to 60 moles of ethylene oxide and castor oil and/or hydrogenated castor oil;

(6) Polyol and in particular polyglycerol esters such as for example polyglycerol polyricinoleate, polyglycerol poly-12-hydroxy stearate or polyglyceryl dimerate. Also useful are mixtures of compounds from several of these classes;

(7) Addition products of from 2 to 15 moles of ethylene oxide with castor oil and/or hydrogenated castor oil;

(8) The partial esters of linear, branched, unsaturated and saturated C_{6-22} fatty acids, ricinoleic acid and 12-hydroxystearic acid and glycerol, polyglycerol, pentaerythritol, dipentaerythritol, sugar alcohols (for example sorbitol), sucrose, alkyl glucosides (for example methyl glucoside, butyl glucoside, lauryl glucoside) as well as polyglucosides (for example cellulose);

(9) Mono, di and trialkyl phosphates as well as mono, di and/or tri-PEG-alkyl phosphates and their salts

(10) Wool wax alcohols

(11) Polysiloxane-polyalkyl-polyether copolymers or corresponding derivatives;

(12) Mixed esters of pentaerythritol, fatty acids, citric acid, and fatty alcohol in accordance with German Patent No, 11 65 574 and/or mixed esters of fatty acids with from 6 to 22 carbon atoms, methyl glucose and polyols, preferably glycerol or polyglycerol; and

(13) Polyalkylene glycols.

The addition products of ethylene oxide and/or propylene oxide with fatty alcohols, fatty acids, alkyl phenols, glyceryl mono and diesters as well as sorbitan mono and diesters of fatty acids or castor oil, are known commercially-available products. They are mixtures of homologues whose mean degree of alkoxylation corresponds to the ratio of ethylene oxide and/or propylene oxide to substrate with which the addition reaction is carried out. The $C_{12/18}$ fatty acid mono and diesters of the addition products of ethylene oxide and glycerol are known from German patent No. 20 24 501 as refatting agents for cosmetic preparations.

$C_{8/18}$ alkyl mono and oligoglycosides, their preparation and their use are known from the art. They are prepared in particular by reacting glucose or oligosaccharides with primary alcohols with from 8 to 18 carbon atoms. For the glycoside residue, both monoglycosides in which a cyclic sugar group is bonded to the fatty alcohol through a glycosidic link, as well oligomeric glycosides with a degree of oligomerisation of preferably about 8 are suitable. The degree of oligomerisation is a statistical mean which is based on a homologue distribution that is typical of these technical-grade products.

Typical examples of anionic emulsifiers are soaps, alkylbenzenesulphonates, alkane sulphonates, olefin sulphonates, alkyl ether sulphonates, glycerol ether sulphonates, alpha methyl ester sulphonates, sulphofatty acids, alkyl sulphates, fatty alcohol ether sulphates, glycerol ether sulphates, hydroxy mixed ether sulphates, monoglyceride (ether) sulphates, fatty acid amide (ether) sulphates, mono and dialkyl sulphosuccinates, mono and dialkyl sulphosuccinamates, sulphotriglycerides, amide soaps, ether carboxylic acids and their salts, fatty acid isethionates, fatty acid sarcosinates, fatty acid taurides, N-acylamino acids such as for example acyl lactylates, acyl tartrates, acyl glutamates and acyl aspartates, alkyl oligoglucoside sulphates, protein fatty acid condensates (in particular wheat-based vegetable products) and alkyl (ether) phosphates. Where the anionic surfactants contain polyglycol ether chains, these can have a conventional homologue distribution, or preferably they have a narrowed homologue distribution.

Zwitterionic surfactants can also be used as emulsifiers. Zwitterionic surfactants are surfactant compounds whose molecule contains at least one quaternary ammonium group and at least one carboxylate and one sulphonate group. Especially useful zwitterionic surfactants are compounds known as betaines such as the N-alkyl-N,N-dimethylammonium glycinates, for example trimethylammonium glycinate, cocoalkyldimethylammonium glycinate, N-acylaminopropyl-N,N-dimethylammonium glycinates, for example cocoacyl aminopropyldimethylammonium glycinate, and 2-alkyl-3-carboxymethyl-3-hydroxyethylimidazolines with from 8 to 18 C atoms in the alkyl or acyl group as well as cocoacylaminoethylhydroxyethyl carboxymethyl glycinate. Especially preferred is the fatty acid amide derivative known by the CTFA name Cocoamidopropyl Betaine. Ampholytic

surfactants are also useful emulsifiers. Ampholytic surfactants are surface-active compounds which in addition to a $C_{8/18}$ alkyl or acyl group in the molecule, also contain at least one free amino group and at least one -COOH- or -SO_3H- group and which are capable of forming internal salts. Examples of useful ampholytic surfactants are N-alkyl glycines, N-alkyl propionic acids, N-alkyl aminobutyric acids, N-alkyl iminodipropionic acids, N-hydroxy ethyl-N-alkylamidopropylglycines, N-alkyl taurines, N-alkyl sarcosines, 2-alkylamino-propionic acids and alkyl aminoacetic acids with from 8 to 18 C atoms in the alkyl group. Especially preferred ampholytic surfactants are N-cocoalkylaminopropionate, cocoacyl-aminoethylaminopropionate and $C_{12/18}$-acyl sarcosine. As well as the ampholytic materials, quaternary emulsifiers can also be used, with materials of the ester quat type, preferably methyl-quaternised difatty acid triethanolamine ester salts, being especially preferred. Typical examples of anionic emulsifiers are alkyl sulphates, alkyl ether sulphates, and monoglyceride (ether) sulphates. As a rule, the active agents and the emulsifiers are used in a weight ratio of from 1:100 to 100:1, preferably from 1:25 to 25:1 and more particularly from 1:10 to 10:1. Especially preferred are those emulsifiers that are capable of forming microemulsions.

Suitable protective colloids are for example gelatine, casein, gum arabic, lysalbic acid, starch, carboxymethylcellulose or modified carboxymethyl cellulose as well as polymers such as for example polyvinyl alcohols, polyvinylpyrrolidones, polyalkylene glycols and polyacrylates.

A further object of the invention is therefore the use in accordance with the invention of nanoscale antimicrobial active agents in which the nanoparticles are coated with one or more emulsifiers and one or more protective colloids.

The nanoparticles of the invention can be prepared for example by
(a) introducing the active agents into a liquid phase in which they are insoluble
(b) heating the resulting mixture above the melting point of the agents
(c) adding to the resulting oil phase an effective amount of at least one emulsifier and finally,
(d) cooling the emulsion below the melting point of the agents.

The invention therefore also relates to the use in accordance with the invention of nanoscale antimicrobial agents which are obtained by this method.

Another process for the preparation of nanoparticles by the rapid expansion of supercritical solutions (RESS) is for example known from the article by S. Chihlar, M. Türk and K. Schaber in Proceedings World Congress on Particle Technology 3, Brighton, 1998. To prevent the nanoparticles from agglomerating, it is advisable to dissolve the starting materials in the presence of suitable protective colloids or emulsifiers and/or to expand the critical solutions into aqueous and/or alcoholic solutions of the protective colloids or emulsifiers or into cosmetic oils which may in turn contain dissolved emulsifiers and/or protective colloids.

Another suitable process for the production of nanoscale particles is the evaporation technique. Here, the starting materials are first dissolved in a suitable organic solvent (for example alkanes, vegetable oils, ethers, esters, ketones, acetals and the like). The resulting solutions are then introduced into water or another non-solvent, generally in the presence of a surface-active compound dissolved therein, such that homogenization of the two immiscible solvents causes the precipitation of nanoparticles, the organic solvent preferably evaporating off. O/W emulsions or O/W microemulsions may be used instead of an aqueous solution. The emulsifiers and protective colloids mentioned at the beginning may be used as the surface-active compounds. Another method for the production of nanoparticles is the GAS (gas anti-solvent recrystallization) process. This process uses a highly compressed gas or supercritical fluid (for example carbon dioxide) as a non-solvent for the crystallization of dissolved substances. The compressed gas phase is introduced into the primary solution of the starting materials and is absorbed therein so that the liquid volume increases, solubility falls, and fine particles are precipitated out.

The PCA process (precipitation with a compressed fluid anti-solvent) is also suitable. In this process, a primary solution of the starting materials is introduced into a supercritical fluid and there are formed extremely finely-divided droplets in which diffusion processes take place, with the result that very fine particles are precipitated out. In the PGSS (particles from gas-

saturated solutions) process, the starting materials are molten by the introduction of gas under pressure (for example carbon dioxide or propane). Temperature and pressure reach near- or super-critical conditions. The gas phase dissolves in the solid and lowers the melting temperature, the viscosity and the surface tension. On expansion through a nozzle, very fine particles are formed as a result of cooling effects.

These processes for the production of the nanoparticles of the invention should be understood as examples only and they do not limit the invention in any way.

The amount of nanoscale compounds used is selected such that the concentration of the antimicrobial agents contained in the nanoparticles is generally of the order of from 0.001 to 5, preferably from 0.01 to 2 and more particularly from 0.1 to 1% by weight, calculated on the preparations.

The oral and/or dental care compositions obtained with the use in accordance with the invention of the nanoscale antimicrobial agents can take the form of toothpastes, gels, liquid dental creams, tooth powders, mouthwashes, as well as chewing products such as chewing gum. Preferably, however, they are in the form of more or less flowable or plastic toothpastes of the type used to clean the teeth with the aid of a toothbrush.

The toothpastes or liquid dental creams of the invention contain a polish, normally in an amount of from 5 to 50% by weight, as well as a humectant, usually in an amount of from 10 to 60% by weight.

As polishes there are suitable any abrasives that are known for toothpastes, such as for example silica gels, aluminium hydroxide, aluminium oxide, calcium pyrophosphate, chalk, dicalcium phosphate dihydrate, sodium aluminium silicates for example zeolite A, organic polymers, for example polymethacrylate, or mixtures of these abrasives. It has been found particularly useful to add a polish that has a restoring action on lesions and open dental canaliculi, namely dicalcium phosphate dihydrate. Dicalcium phosphate dihydrate ($CaHPO_4$ ·

$2H_2O$) occurs naturally as Brushite and is available in commerce in suitable particles sizes of between 1 and 50 μm.

A combination of humectants, binders and water is suitable as the vehicle for the toothpastes of the invention, which is used to obtain a suitable consistency for dispensing the pastes from tubes, dispensers or flexible bottles. The humectant can for example be glycerol, sorbitol, xylitol, propylene glycols, polyethylene glycols, in particular those with mean molecular weights of from 200 to 800. As consistency regulators (or binders) there can be used for example natural and/or synthetic water-soluble polymers such as alginates, carragheenates, tragacanth, starch and starch ethers, cellulose ethers such as for example carboxymethyl cellulose (Na salt), hydroxyethyl cellulose, methylhydroxypropyl cellulose, guar, acacia gum, agar-agar, xanthan gum, succinoglycan gum, locust bean gum, pectins, water-soluble carboxyvinyl polymers (for example Carbopol® grades), polyvinyl alcohol, polyvinylpyrrolidone, polyethylene glycols, in particular those with molecular weights between 1,500 and 1,000,000.

Other substances that are suitable for controlling viscosity are for example sheet silicates such as for example montmorillonite clays, colloidal thickening silica gels such as for example Aerogel silica gels, pyrogenic silica gels, and very finely-divided precipitated silica gels.

The viscosity of the toothpastes can also be adjusted to be sufficiently low for them to be dispensed in the form of "liquid dentifrices" with a viscosity of from 2000 to 40,000 mPas (25 °C) from a flexible plastics bottle onto a toothbrush, where they penetrate between the bristles but do not drip off the brush. For this purpose, there is preferably used as the binder or excipient a combination of from 0.1 to 1% by weight of xanthan gum and/or carboxymethylcellulose and from 0.01 to 5% by weight of a viscosity-stabilising additive selected from the group of

- cationic, zwitterionic and ampholytic nitrogen-containing surfactants
- hydroxypropyl-substituted hydrocolloids
- polyethylene glycol/polypropylene glycol copolymers with a mean molecular weight of from 1000 to 5000

or a combination of the aforesaid compounds.

The toothpastes of the invention also contain surface-active substances in amounts of from 0.1 to 5% by weight in order to enhance the cleaning action and if desired to generate foam during toothbrushing, and also to stabilise the dispersion of polishing agent in the vehicle. Useful surfactants are for example linear sodium alkyl sulphates with from 12 to 18 C atoms in the alkyl group. These substances additionally have an enzyme-inhibiting action on the bacterial metabolism of dental plaque. Other suitable surfactants are the alkali metal salts, preferably the sodium salts, of alkyl polyglycol ether sulphates with 12-16 carbon atoms in the linear alkyl group and 2-6 glycol ether groups in the molecule, of linear (C_{12}-C_{18}) alkane sulphonates, sulphosuccinic acid (C_{12}-C_{18})-monoalkyl esters, sulphated fatty acid monoglycerides, sulphated fatty acid alkanolamides, sulphoacetic acid (C_{12}-C_{16})-alkyl esters, acyl sarcosines, acyl taurides and acyl isethionates with 8-18 carbon atoms in the acyl group. Zwitterionic, ampholytic and nonionic surfactants are also suitable, for example the ethoxylates of fatty acid mono and diglycerides, fatty acid sorbitan esters and alkyl (oligo)-glucosides.

Other conventional toothpaste additives are

- sweeteners such as for example saccharin sodium, sodium cyclamate, sucrose, lactose, maltose, fructose,
- flavourings such as for example peppermint oil, spearmint oil, eucalyptus oil, aniseed oil, fennelseed oil, caraway oil, methyl acetate, cinnamaldehyde, anethol, vanillin, thymol, as well as mixtures of these and other natural and synthetic flavourings,
- Pigments such as for example titanium dioxide
- Dyes
- Buffers such as primary, secondary and tertiary alkali metal phosphates or citric acid/sodium citrate
- Healing and anti-inflammatory substances such as for example allantoin, urea as well as azulene, camomile active agents, acetylsalicylic acid derivatives.

In mouthwashes, the vehicle essentially consists of water, ethanol, essential oils, emulsifiers, and solubilisers for the remaining flavour components, taste improvers (e.g. sweetener), and optionally astringent or stimulating drug extracts and optionally dyes.

To prepare the oral and/or dental care compositions of the invention, the nanoscale antimicrobial agents are mixed together with the remaining components of the formulation in the known manner.

Therefore, the invention further relates to oral and/or dental care compositions containing antimicrobial agents that are characterised in that the antimicrobial agent is incorporated in the form of nanoparticles having a particle diameter in the range from 5 to 500 nm and preferably from 10 to 150 nm.

Other aspects and/or embodiments are evident from the subclaims.

Examples

The examples following herebelow describe the invention in greater detail.

Example 1

Preparation of nanoscale salicylic acid N-octylamide

0.5 g of salicylic acid N-octylamide (MP about 45 °C) were dissolved in 100 g of deionised water and the mixture was heated to about 50 °C, to form a two-phase mixture comprising a water phase and an amide phase. The latter was emulsified by adding 8.9 g of alkyl ether sulphate (Texapon ® N 70, Henkel KGaA, Düsseldorf), whereupon a clear mixture was formed. The gradual transition of the oil phase into the transparent water/amide/emulsifier mixture can be treated as an indication that a microemulsion has been formed. The microemulsion was cooled, with continuous stirring, to ambient temperature and was then evaporated to dryness in the rotary evaporator, furnishing 9.4 g of nanoparticulate salicylic

acid N-octylamide enclosed in the ether sulphate matrix. It was possible to make the nanoparticles into a stable transparent dispersion again by adding ten times their quantity of water. For light refraction, the particles exhibited a maximum at a particle size of 120 nm after numerical weighting.

Example 2

Preparation of a nanoscale aqueous salicylic acid-N-octylamide dispersion

1.0 g of salicylic acid N-octylamide (MP about 45 °C) were emulsified, with slow heating to 52 °C, with 30 g of deionised water, 30 g of polydiol 400 (PEG 8) and 2 g of polyoxyethylene glycerol fatty acid ester (Tagat S). Thereafter 30 g of fatty acid amidoalkylbetaine (Tego Betain BL 215) were added and a clear stable dispersion was formed. The dispersion was then allowed to cool to room temperature. There were obtained 93 g of a transparent dispersion. The particles exhibited a maximum of light refraction at a particle size of 15 nm, after numerical weighting.

The nanoscale salicylic acid N-octylamide obtained in Examples 1 and 2 was used to prepare the following oral and/or dental care compositions (all figures are percentages by weight):

Examples 3 to 6

Toothpastes

	3	4	5	6
Precipitated silica: Sident ® 12 DS	10.0	12	15	18
Precipitated silica: Sipernat ® 22 LS	3.0	3.0	-	-
Alumina Polish ultrafine (1)	-	-	-	10
Dicalcium phosphate dihydrate	4.0	4.0	-	-
$MgSO_4 \cdot 7H_2O$	1.7	1.4	-	-
Na monofluorophosphate Na_2PO_3F	1.2	0.8	0.5	0.6
KNO_3 (anhydrous)	5.0	4.0	4.5	3
Glycerol (86% DAB)	21.0	18.0	10.0	17.5
Sorbitol (70% DAB)	20.0	14.0	5	17.5
Polyethylene glycol (mol. wt.: 400)	2.0	2.0	1.0	1.0
Thickening silica gel (FK 320 DS)	1.0	1.0	5.0	0.8
Xanthan gum (Keltrol ® F)	0.6	0.6	0.6	0.5
Titanium dioxide	1.0	1.0	-	-
Na lauryl sulphate	1.5	1.5	-	2.0
Tego Betain BL 215 (2)	0.6	0.6	-	-
Trisodium citrate	0.2	0.2	-	-
Saccharin Na	0.2	0.2	0.1	0.2
Nano salicylic acid N-octylamide of Example 1	1.0	2.0	1.5	2.0
Flavour	1.0	0.8	0.1	1.0
Cremophor RH60 (3)	-	-	0.2	-
Water	to 100	to 100	to 100	to 100

Example 7

Liquid dental cream

	7
Precipitated silica (Sident 12 DS)	12.0
NaF	0.25
KNO_3	5.0
Na_2HPO_4	0.2
Xanthan gum (Keltrol F)	0.2
Azacycloheptane-2,2-diphosphonate (Na salt)	1.0
Saccharin Na	0.2
Ethanol	5.0
Glycerol	28.0
Sorbitol	22.0
Polyethylene glycol (mol wt: 400)	3.0
PEG 30 - glyceryl monostearate	1.0
Tego Betain BL 215 (2)	0.8
Flavouring oil	1.0
Nano salicylic acid N-octylamide of Example 1	2.0

Example 8

Mouthwash (ready to use)

	8
Ethanol	5.0
Chlorhexidine gluconate	0.03
Plantaren 2000 (4)	0.05
Na_2PO_3F	0.25
KNO_3	4.0
Saccharin Na	0.05
Sorbitol	3.0
Cremophor RH 60 (3)	0.1
Flavouring oil (peppermint oil)	0.1
Nano salicylic acid N-octylamide of Example 2	3.0
Dye (Blue CJ 42090)	0.1
Water	to 100

The following commercial products were used:

(1) Alumina Polish P10: lightly calcined alumina

(about 20% by weight of gamma-aluminium oxide, about 80% by weight of alpha-aluminium oxide; primary crystal size 0.5 to 1.5 μm)

(2) Tego ® Betain BL 215: 30% solution of cocoamidopropyl-betaine in water

(3) Cremophor ® RH 60: hydrogenated castor oil + 60 moles EO

(4) Plantaren 2000: alkyl-(C_8-C_{16}-oligo-(1,4)-glucoside (50% solution in water).

Patent claims

1. The use of nanoscale antimicrobial agents having a particle diameter in the range from 5 to 500 nm for the preparation of oral and/or dental care products.

2. The use according to Claim 1 characterised in that the agents are sparingly water-soluble compounds.

3. The use according to Claim 1 characterised in that the agents are not basic compounds.

4. The use according to at least one of claims 1 to 3 characterised in that the active agents used are selected from the group comprising 4-hydroxybenzoic acid and its salts and esters, N-(4-chlorophenyl)-N'-(3,4-dichlorophenyl)-urea, 2,4,4'-trichloro-2'-hydroxydiphenyl ether,

4-chloro-3,5-dimethylphenol, 2,2'-methylene-bis-(6-bromo-4-chlorophenol), 3-methyl-4-(1-methylethyl)phenol, 2-benzyl-4-chlorophenol, 3-(4-chlorophenoxy)-1,2-propanediol, 3-iodo-2-propinylbutylcarbamate, vitamin A palmitate, thymol, salicylic acid N-alkyl amides, and mixtures thereof.

5. The use according to at least one of Claims 1 to 4 characterised in that salicylic acid octylamide and/or salicylic acid n-decylamide is used.

6. The use according to at least one of claims 1 to 5 characterised in that there are used nanoscale agents that are obtained by
(a) introducing the agents into a liquid phase in which they are insoluble
(b) heating the resulting mixture above the melting point of the agents
(c) adding to the resulting oil phase an effective amount of at least one emulsifier or protective colloid and finally,
(d) cooling the emulsion below the melting point of the agents.

7. The use according to at least one of claims 1 to 6 characterised in that there are used nanoparticles that are coated with one or more emulsifiers and/or protective colloids.

8. The use according to at least one of claims 1 to 7 characterised in that the nanoscale agents are used in such amounts that the concentration of the antimicrobial agents contained in the nanoparticles is from 0.001 to 5% by weight, calculated on the preparations.

9. The use according to at least one of claims 1 to 8 characterised in that the nanoscale agents are used to prepare toothpastes or dental gels.

10. Oral and/or dental care compositions containing antimicrobial agent, characterised in that the antimicrobial agent is incorporated in the form of nanoparticles having a particle diameter in the range from 5 to 500 nm.
